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Post-Stroke Aphasia Rehabilitation: A Review of the History and Findings for Constraint-Induced Therapy

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Post-Stroke Aphasia Rehabilitation: A Review of the History and Findings for Constraint-Induced Therapy

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Report

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Abstract

Post-Stroke Aphasia Rehabilitation: A Review of the History and Findings for Constraint-Induced Therapy

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Abstract: Constraint-induced (CI) therapy is an approach adapted from motor rehabilitation to treat language deficits in individuals with poststroke aphasia. The principles of CI therapy were established from behavioral research with animal models that were later applied to human neurorehabilitation. There is a substantial body of evidence to support CI therapy for the treatment of postroke motor deficits; however, evidence for CI aphasia therapy is less established. This report examines the history and current state of evidence for the use of CI-based therapy to treat adults with poststroke aphasia.

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Chapter 1: Introduction

According to a report by the American Heart Association, every 40 seconds, a person in the United States will experience a stroke (Lloyd-Jones et al., 2009). Approximately one in five of these individuals will develop poststroke aphasia (PSA), resulting in deficits in language comprehension and/or verbal expression (Lloyd-Jones et al., 2009). Directly following a cerebral vascular incident, an individual's verbal communication is extremely sparse (Berthier & Pulvermüller, 2011). However, after a period of several weeks to months, aphasia symptoms typically dissipate during a period of spontaneous neurological recovery (Berthier & Pulvermüller, 2011). Communication deficits that persist following poststroke aphasia (PSA) may lead to increased isolation, passiveness and depression, which may further contribute to physiological and psychiatric symptoms (Starkstein & Robinson, 1988; as cited in Berthier & Pulvermüller, 2011). While spontaneous improvements beyond the acute stages of recovery are rare, (Berthier & Pulvermüller, 2011), there is evidence to suggest that individuals in the chronic stages of aphasia may benefit from intensive therapy (Basso & Macis, 2011).

Constraint-Induced (CI) therapy to treat symptoms of poststroke aphasia was introduced approximately a decade ago by Pulvermüller and colleagues. The principles of CI based approaches evolved from behavioral research with animals, and later were applied to physical rehabilitation in humans to treat motor impairments resulting from central nervous system damage (Meinzer, Rodriguez & Rothi, 2012). Subsequent modifications of the approach have been utilized to target individualized language deficits and to treat individuals in the acute stages of aphasia. CI-based approaches also have been employed in functional imaging studies to investigate treatment-induced neurological changes beyond the stage of spontaneous recovery. The aim of this report is to review the history and current state of evidence for the use of CI-based therapy to treat adults with poststroke aphasia.

Chapter 2: History of Constraint-induced therapy

Though CI-based therapy is a relatively new treatment approach, the underlying principles are rooted in behavioral neuroscience dating back over a century. Animal studies exploring the motor effects of surgically induced somatosensory deafferentation provide the earliest evidence for the learned nonuse model on which CI therapy is based. Most prominently, Edward Taub (1977; 1980) was the first researcher to establish and test the learned nonuse model in animal subjects and apply his findings to human rehabilitation.

Somatosensory deafferentation is a surgical procedure that involves serially sectioning all of the dorsal roots of the spinal cord that innervate a given body part, such as a limb (Taub, 1977). Through this process, spinal reflexes and afferent pathways that provide somatosensory feedback from the limb to the brain are permanently abolished, while motor innervation remains intact (Taub, 1977). Extensive research has been conducted with animals to establish the necessity of somatosensory feedback and spinal reflexes in performance of various movements. Subsequent behavioral research using deafferentation procedures additionally explored the role of somatosensory feedback in various types of learning (Taub, 1980).

Prominent differences in movement patterns emerge when bilateral and unilateral forelimb deafferentation is carried out in rhesus monkeys (Taub, 1980). Following bilateral forelimb deafferentation, a monkey will continue to make use of both affected limbs after a period of recovery, despite reduction in coordination and precision (Taub, 1977). In contrast, when a unilateral limb is deafferented, the monkey ceases to use the affected limb indefinitely and instead relies solely on its unaffected limbs when left in a free environment (Taub, 1980).

Knapp, Taub and Berman (1958) initiated a series of experiments investigating the use of conditioning techniques to stimulate movement in a deafferented limb that would not otherwise occur spontaneously (as cited in Taub, 1980). Conditioned response (CR) procedures incorporated several key features: 1) an increase in motivation to use the limb that could be controlled in a defined manner and maintained at a high level over an extended period of time 2) motor requirements that were simple in nature, and 3) repeated trials with consistent performance criteria to establish many opportunities for learning and achieving the desired behavioral outcome (as cited in Taub, 1980).

Applying these feature in their experimental design, Knapp, Taub and Berman (1958) found that purposive movement could be induced under restricted conditions when a) the intact limb was immobilized using a straitjacket, and b) the monkey was placed in a conditioned-response situation requiring the limb to be flexed at the onset of auditory stimulus in order to avoid an electric shock (as cited in Taub, 1980). Using shaping techniques, in which behavioral objectives were increased in small increments gradually over a period of massed practice, the monkeys were able to regain movement in their affected limbs (Taub, 1977). Similar outcomes also were achieved in studies involving instrumental conditioning of deafferented limbs of cats, rodents and dogs (Gorska & Jankowska, 1961; Konorski, 1962).

However, maintenance of conditioning was not achieved in Knapp, Taub, and Berman's (1958) preliminary study. A return to nonuse of the affected limb was observed following removal of the immobilizing device shortly after purposive movement was achieved. Consequently, a second experiment was conducted, in which the duration of restraint of the intact limb was increased to three days (Taub, 1980). The restraint period was also delayed until nine week post-operation, compared to two weeks in the initial experiment (Taub, 1980). In contrast with previous findings, the monkeys maintained use of the deafferented limb following removal of the immobilizing device in a similar manner to the bilaterally deafferented monkeys (Taub, 1980).

THE LEARNED NONUSE MODEL

Taub (1977) suggested that the contrast in findings of the two experiments was evidence for a learning phenomenon that he coined the *learned nonuse hypothesis.* Immediately following the deafferentation procedure, monkeys cannot make use of their affected limbs, as recovery of function requires considerable time. This period of reduced functioning following neurological damage to the spinal cord is known as spinal shock. During this time, the background level of excitability of motor neurons is depressed. Following injury, the threshold for excitation required to produce movement is elevated significantly, but gradually decreases back to normal levels over a period of recovery. This gradual recovery of function has been evidenced in bilateral deafferentation studies, with a period of spinal shock lasting from two to six months for monkeys.

Taub (1980) observed that monkeys with unilaterally deafferented limbs make immediate attempts to utilize the deafferented limb following surgery, despite depressed functioning. However, these attempts are unsuccessful in the early stages of recovery and the monkey gradually learns that use of the limb contributes to aversive consequences and ceases attempts to use the limb. This learned nonuse persists even when the potential for movement is regained. Moreover, motivation to use the affected limb decreases over time, as the monkey is able to function effectively by using its intact limbs for ambulation and purposive movements, therefore positively reinforcing the behavior of nonuse. In contrast, the monkeys with bilaterally deafferented limbs maintain high levels of motivation to use their affected extremities, and as soon potential for use is regained, the limbs are utilized.

Taub (1980) explained that the monkey's motivation to use a unilaterally deafferented limb could be increased sharply by immobilizing the intact limb for a period of months following surgery, thereby overcoming learned nonuse of the limb. Once purposive movement was achieved through conditioning and shaping techniques, these learned behaviors also required strengthening over a period of several days in order to be maintained following removal of the immobilizing device. By strengthening use of the affected limb, the animal may successfully overcome the learned nonuse behavior when restrictive conditions are removed.

Additional experiments conducted by Taub (1977) lend support for the learned nonuse hypothesis. In subsequent experiments, restraint of the deafferented limb was initiated while several monkeys were still under anesthesia to prevent movement of the deafferented limb for a period of three months. This prevented the monkeys from attempting to use their deafferented limbs while motor function was depressed and learning that the limb could not be used effectively. Under this condition, Taub speculated that learned nonuse could be prevented from developing and strengthening during the period of spinal shock. As predicted, the animals were able to use their deafferented limb following removal of the immobilizing device three months after the surgery.

FORCED OVERUSE

Although the studies presented suggest that constraint techniques may be therapeutic in overcoming learned nonuse, additional animal studies investigating "forced overuse" suggest that implementation too early and rigorously in the early recovery process may have harmful effects (Kozlowski & Schallert, 1996; Humm, Kozlowski, James, Gotts, & Schallert, 1998). In studies of forced overuse, researchers restrained the unaffected limb in a plaster cast immediately following a sensory motor cortex lesion for 14 days. Results indicated that forced overuse of the affected limb during the first week following surgery hindered motor recovery and even increased lesion size. When restraint was deferred an additional week, enlargement of the lesion site was not observed, however negative impacts on behavioral recovery were observed. Similar findings of impaired sensorimotor recovery and enlarged lesion site were demonstrated in rats with middle cerebral infarcts (Bland et al., 2000). Such studies suggest potential risks of beginning CI-based approaches in the acute stages following stroke.

In summary, animal studies provided the first evidence to suggest that motor deficits resulting from central nervous system damage may persist due to the phenomenon of learned nonuse. Taub (1977; 1980) demonstrated that conditioning techniques involving constraint of the unaffected limb could be employed to overcome learned nonuse in animals. However, additional studies involving rats (Kozlowski & Schallert, 1996; Humm, Kozlowski, James, Gotts, & Schallert, 1998) suggested constraint-based techniques may produce harmful effects if applied too early in recovery.

Chapter 3: Application to Movement Disorders in Humans

Taub (1980) was one of the first researchers to apply his findings on learned nonuse in animals to human medicine. Following brain injury or stroke, humans also undergo a period of temporary, organically-based inability to use an affected upper limb as a result of central nervous system (CNS) shock (Taub, 1977). During the period of initial CNS shock state, learned nonuse may develop as a result of unsuccessful attempts to use an affected limb (Taub et al., 1993). However, if a sufficient neural substrate remains intact following the infarct to provide a basis for movement, learned nonuse may be overcome once initial CNS shock has subsided (Taub et al., 1993). By utilizing constraint techniques that obligate repeated use of the affected limb, cortical reorganization may be stimulated to build a foundation for recovery of movement following the injury.

Building on the work from a pilot study conducted by Wolf, Lecraw, Barton and Jann (1989) and the findings from his animal research, Taub and colleagues (1993) conducted the first experimental study of constraint-induced movement therapy (CIMT) to treat motor deficits in nine individuals with chronic strokes. Participants randomly assigned to the experimental group were required to wear a movement restriction device, consisting of a resting hand splint placed in a sling, on the contralateral limb for 90% of waking hours for a period of 12 days. During the eight weekdays during this intervention period, participants attended six hours of daily rehabilitation in which they participated in activities that required use of the paretic upper extremity in behaviorally relevant contexts (e.g. eating lunch with fork and knife; playing dominos, throwing a ball; playing card games). Participants were required to practice tasks repeatedly, with the purpose of gaining experience using the affected arm (as cited in Taub & Wolf, 1997). Participants in the comparison group received physical therapy and at-home exercises that involved passive movements of the affected limb, rather than stimulating purposive movement. Tests of motor function were administered pre- and post-intervention, revealing significant and substantial effects for the experimental group. Improvements were observed on simple limb movements and complex tasks involving completion of activities of daily living. Transfer of motor function to tasks in the home environment was also observed and maintained for two years following the intervention period, as measured using the Motor Activity Log (MAL) (Uswatte, Taub, Morris, Light, & Thompson, 2006).

Since Taub and colleagues' (1993) preliminary study, a substantial body of research including several large-scale clinical trials, has investigated the efficacy of CIMT (Meinzer, Rodriguez, & Rothi, 2012). Variations of the original protocol have been applied in treating individuals with post-stroke motor impairments, partial spinal cord injury and traumatic brain injury (Taub, Uswatte, & Pidikiti, 1999). Although shaping was not an original component of the treatment, subsequent studies have employed successive approximation procedures and other shaping techniques in a highly intensive training environment to achieve behavioral motor objectives (Grotta et al., 2004). Additionally, restraint devices have been expanded across studies to include less obstructive forms of restraint, such as mitts and gloves (Tuke, 2008).

CIMT has been utilized with patients across chronic, subacute and acute stages of stroke (Tuke, 2008). However, the majority of studies of CIMT have included participants in chronic and subacute stages of stroke recovery (Grotta et al., 2004). Despite implications of potential harmful effects seen in animal studies in which CI therapy was employed too soon following injury, no serious adverse affects were noted in studies of acute stroke (Tuke, 2008). Though CIMT is becoming an increasingly well-established form of treatment for stroke-induced motor impairments, optimal level, distribution and timing of CIMT input remain unclear as a result of lack of standardization across studies (Tuke, 2008). Overall, CIMT has been shown to improve upper and lower extremity motor impairments in individuals with chronic strokes (Taub, Uswatte, & Elbert, 2002; Carter, Conner, & Dromerick, 2010). Furthermore, functional imaging has shown that CIMT is associated with cortical reorganization of networks supporting motor functioning (Taub, Uswatte, & Pidikiti, 1999).

Chapter 4: Extending CI Principles to Aphasia Therapy

Substantial evidence supporting the modifiability of motor behavior following constraint-induced therapy led to speculation about the application of similar techniques to modify speech output in individuals with chronic aphasia (Pulvermüller et al., 2001). Constraint-induced aphasia treatment (CIAT), also called constraint-induced language treatment (CILT) or intensive language-action therapy (ILAN), was first introduced by Pulvermüller and colleagues (2001) to train individuals with aphasia to overcome learned nonuse of spoken communication following stroke.

Individuals with aphasia tend to rely heavily on communication strategies that require the least amount of effort (Pulvermüller et al., 2001). While speaking, they tend to use familiar words and phrases that can be produced easily and avoid forms of verbal output that they anticipate to be more difficult (Pulvermüller et al., 2001). Gestures and drawings are often used in place of verbal output and withdrawal from communication is common (Pulvermüller et al., 2001). Pulvermüller et al. (2001) were the first to suggest that these compensatory strategies and changes in communication patterns constitute a form of learned nonuse. Nonuse behaviors may develop in the early stages of aphasia in response to initial speech difficulties (Szaflarski et al., 2008). Negative feedback from friends and family and personal feelings of embarrassment or inadequacy may reinforce avoidance and cause nonuse behaviors to persist (Szaflarski et al., 2008)

Pulvermüller and colleagues (2001) developed the first treatment protocol to directly address learned nonuse in aphasia using the same overarching principles utilized in CIMT: massed practice, constraint induction, shaping and behavioral relevance. An intensive therapy schedule (3-4 hrs/day) is utilized over a period of several weeks (massed practice). Patients' communication modality is restricted to spoken language (constraint induction) to limit use compensatory nonverbal behaviors. Modifications to communication behaviors are introduced gradually (shaping) to reduce frustration and repeated failure. Lastly, therapy is conducted in a communicative setting that is behaviorally relevant to the individual's everyday life (behavioral relevance) in order to promote generalization.

THERAPY PROTOCOL

Therapy activities consist of therapeutic barrier games resembling the card game "go fish" conducted between a therapist and up to three patients (Meinzer, Rodriguez & Rothi, 2012). At the beginning of the game, the therapist distributes pairs of cards depicting drawings of objects, written words, or drawings/photographs of complex activities of daily living (Meinzer, Rodriguez, & Rothi, 2012). Increasingly complex cards may be utilized to shape the difficulty of the task (Meinzer et al., 2007). Cards may consist of: 1) objects that require descriptions using high- or low-frequency words in the language, 2) objects with phonologically similar names (i.e. minimal pairs) that require exact articulation 3) the same object with varying descriptive features (e.g. color or number) requiring more elaborate explanations (Meinzer et al., 2007). Cards are allocated in manner so that no player has two identical cards (Meinzer, Rodriguez, & Rothi, 2012). Cards are typically placed in front of the players, with barriers set up between the players to conceal their cards from the other group members (Meinzer, Rodriguez, & Rothi, 2012).

The game requires players to take turns selecting one of their cards and asking another player if he or she possesses the corresponding match (Meinzer, Rodriguez, & Rothi, 2012). Both players must verbally engage during this exchange using spoken words or sentences to either request, respond, or reply (Meinzer, Rodriguez, & Rothi). Constraints are individually determined based on the participant's verbal skills at initial testing (Meinzer et al., 2007). For example, an highly nonfluent individual may be allowed to use approximations of relevant utterances limited to one to two word utterances, while less severely impaired individuals may be required to use clear articulation and address a co-player using politeness formulas or syntactically correct sentences (Meinzer et al., 2007). In some studies, constraint to spoken output was strictly enforced, to the extent that players were required to sit on their hands to avoid gesturing (Meinzer, Rodriguez, & Rothi, 2012). Other studies permitted the use of gestures (Meinzer et al., 2007; Meinzer, Streiftau, & Rockstroh, 2007) as a facilitator for language processing (Meinzer et al., 2011; as cited in Meinzer, Rodriguez & Rothi, 2012). A second therapist is typically present to assist during the game by providing positive reinforcement and prompts as needed (Meinzer, Rodriguez & Rothi, 2012). As the participants' language skills improve, the complexity of material is increased and performance requirements become more challenging (Meinzer, Rodriguez, & Rothi, 2012). For example, initial card sets may contain objects that may describe using high-frequency words, while later card sets may include minimal pairs or similar objects that vary in number or color and require more detailed descriptions (Meinzer et al., 2007). Through gradual shaping, the participants' are encouraged to use the highest language within their skill range to progressively increase expressive language skills (Meinzer, Rodriguez, & Rothi, 2012).

Chapter 5: Evaluation of CI Therapy in Chronic Aphasia

Pulvermüller and colleagues (2001) preliminary study laid the groundwork for future studies of CIAT with individuals with chronic stroke. In their preliminary study, 17 participants with moderate to severe chronic aphasia (<12 months poststroke) were selected for treatment. Ten participants were randomly assigned to the CI treatment group, while the remaining seven were assigned to a control group to receive traditional aphasia therapy. Participants in the CI group received 30 total hours of therapy, distributed over 10 consecutive days of three-hour sessions. Participants in the control group received the same amount of therapy over a duration of three to five weeks. Prior to therapy and following intervention, all participants were required to complete comprehensive standardized language testing using the Aachen Aphasia Test (AAT) (Huber, Poeck, Weniger, Willmes, 1983). Additionally, they completed a questionnaire regarding their amount of communication and comprehension in daily communication (Communicative Activity Log (CAL) (Pulvermüller, 2001) during these two periods. The CAL was developed as a similar tool as the Motor Activity Log (MAL; Uswatte, Taub, Morris, Light, & Thompson, 2006) utilized in CIMT studies. The CAL contains 46 questions to be completed using 6-point rating scale. The questionnaire contains two scales to assess amount and quality of day-to-day communication as measured by self-rating and ratings of outside therapists not involved in the intervention. Following intervention, significant language improvements were found only for the CIAT treatment group, as measured by average weighted scores on the Token Test, naming, comprehension and repetition AAT subscales. Comparatively, the traditional therapy group demonstrated improvements only on the naming test. Significant improvements also were noted on the CAL for the CIAT treatment group, as measured by increase in amount of daily communication. The significant improvements for the CIAT group was particularly notable given that the average time post-stroke was significantly longer for the treatment group compared to the control group (mean, 98.2 vs 24 months). However, no follow-up data was collected to assess maintenance of treatment gains over time.

Meinzer, Djundja, Barthel, Elbert, and Rockstroh (2005) found evidence to support the use of CIAT with individuals with chronic aphasia. Twenty-seven individuals with chronic stroke (time poststroke: 13-116 months) participated in their study. Participants were diagnosed primarily as having Broca's aphasia (n=11) or Wernicke's aphasia (n=7). Treatment was conducted over a span of ten days, with a total of 30 therapy hours provided. Approximately half of the participants were assigned to receive an additional home training program (CIATplus group) completed in the afternoon of each training day. Home exercises, consisting of daily communication practice with a family member, were designed to progressively increase communication during the participants' daily interactions to promote carryover. The AAT (Huber, Poeck, Weniger, Willmes, 1983) and CAL (Pulvermüller, 2001) were used as assessment measures pre- and post-intervention, and at a follow-up assessment conducted six months after termination of treatment. Significant improvements, demonstrated in at least one substest or subscale of the AAT, were found for 85% of participants (Meinzer, Rodriguez, & Rothi, 2012). At follow-up, treatment gains were maintained as compared to baseline assessment measures. Assessments using the CAL revealed increases in the amount of day-to-day communication and comprehension. In addition, the participants' relatives gave improved ratings to their overall communicative effectiveness, as measured using the Communication Effective Index (CETI) (Lomas et al., 1989). No significant differences were found between the CIAT and CIATplus groups at the post-treatment assessment. However, only the CIATplus participants continued to demonstrate further gains in the quality of daily communication (CETI) and only for these participants did the amount of communication and comprehension (CAL) remain higher than baseline at follow-up.

Although these studies provide evidence for the effectiveness of CIAT, they fail to control for the impact of treatment intensity, limiting the ability to draw conclusions on which aspect of therapy contributes most to improved language function (Meinzer, Rodriguez, & Rothi, 2012). A meta-analysis conducted by Kelly, Brady, and Enderby (2010) suggested that other aphasia therapy approaches may also benefit from more intensive treatment schedules (as cited in Meinzer, Rodriguez, & Rothi, 2012). To investigate the effects of treatment intensity on therapy outcomes, CI-based therapy was compared to another high intensity treatment approach, model-oriented aphasia therapy (MOAT) (Barthel, Meinzer, Djundja, & Rockstroh, 2008). The 27 participants from Meinzer and colleagues' (2005) study were compared to a group of 12 participants with chronic aphasia treated with MOAT. No control group was utilized. Participants from both treatment groups were comparable in clinical and sociodemographic characteristics, however differences in lesion size and location across participants were noted. While MOAT also employs the same intensive treatment schedule (3 hrs/day for 10 days), shaping, and a family training component, no constraint is utilized. Additionally, MOAT differs from CIAT in that treatment is provided in an individual setting, with specific therapy approach (e.g. strategy approach, linguistic approach, communicative approach) individually tailored to the individual's deficits in language production. Language functions were assessed using the AAT (Huber, Poeck, Weniger, Willmes, 1983), CAL (Pulvermüller, 2001), and CETI (Lomas et al., 1989) immediately following treatment, and at six months following the training to evaluate for maintenance. Results indicated significant improvements on the AAT for participants in the MOAT group, with comparable results to the CIATplus group across all measures. Improvements were stable at follow-up testing. Findings suggest that treatment intensity and family training were critical components to treatment of chronic aphasia.

To determine whether constraint, or forced use of spoken language modality, is a necessary factor for treatment success, CILT was compared to a multi-modality approach, Promoting Aphasic Communicative Effectiveness (PACE) (Maher et al., 2006). Nine participants were assigned to receive CILT (n=4) or PACE (n=5) over a duration of two weeks (3 hrs/day, 4 days/week). Assignment was not randomized to allow for groups to be matched in terms of aphasia severity and concomitant apraxia of speech. Both approaches were delivered in a group therapy setting and matched for treatment intensity, difficulty of tasks, and communication burdens. A similar card game was used in therapy activities across both approaches, however, the PACE group was allowed to utilize multiple modalities of communication (e.g.

gesturing, writing) to transfer information while the CILT group was constrained to spoken output. Both treatment groups demonstrated improvements on the Boston Naming Test (Kaplan, Goodglass, & Weintraub, 2000), Western Aphasia Battery (Kertesz, 2007), Naming Test (Nicholas et al., 1985) and measures of narrative discourse. However, gains were more pronounced and consistent for the CILT group. Additionally, the participants in the CILT group that demonstrated most substantial improvements continued to maintain gains at follow-up. Results indicate the potential therapeutic effect of forced use of spoken language; however, participants in the PACE group had more severe apraxia of speech which may have been a confounding factor. Sample size was too small to draw definitive conclusions from the results.

A recent study evaluated the effects of constrained versus unconstrained intensive therapy in improving naming for individuals with chronic aphasia and severe nonfluent speech and/or apraxia of speech (AOS) (Andrianopoulus, Burke, Kurland, Pulvermüller, & Silva, 2012). Two participants with chronic moderate-to-severe aphasia and comorbid AOS were treated simultaneously, first using PACE and then with CIAT using a multiple-baseline approach. A picture naming fMRI protocol was conducted at baseline and after each treatment. Results indicated that both participants made greater and faster gains following CIAT treatment compared to PACE. Additionally, functional imaging suggested that improved naming was associated with increased activation of perilesional tissue. Only one participant returned for a follow-up assessment, demonstrating only modest maintenance and reduced generalization to untrained pictures. Results suggest that CIAT may provide a “kick-start” for individuals with aphasia to overcome learned nonuse, but given the short-term intensive nature of the approach, maintenance of gains are limited. Small sample size and the possibility of order effect also should be noted as limitations. Results suggest that CIAT may be effectively used with individuals with concomitant AOS, in addition to chronic aphasia.

In summary, evidence from studies (Pulvermüller et al., 2001; Meinzer et al., 2005; Maher et al., 2006) suggests that CIAT may be effective in improving language functioning for individuals with chronic aphasia. Participants have demonstrated gains on standardized language tests and measures of connected speech and functional communication, with maintenance at follow-up demonstrated in some studies (Meinzer et al., 2005; Maher et al., 2006). Reduced maintenance in other studies (Barthel et al., 2008; Andrianopoulus et al., 2012) suggest the need for a more intensive training schedule and/or a family training component to increase generalization of treatment effects. Evidence about which elements of CIAT, apart from treatment intensity, play a key role in treatment outcomes is limited. Other forms of therapy (e.g. PACE, MOAT) that utilize intensive treatment schedules have demonstrated comparable results to CIAT without the use of constraint (Kurland, Baldwin, & Tauer, 2010; Barthel et al., 2008). While there is preliminary evidence to suggest that constraint of nonverbal communication modalities may improve language functioning, additional research using large-scale clinical trials is necessary to achieve more conclusive evidence of efficacy. Evidence from CIMT suggests that massed practice and shaping are the most critical components of treatment, while constraint plays a relatively minor role (Meinzer, Rodriguez, &

Rothi, 2012). Further investigation into which elements of CIAT (e.g. behaviorally relevant setting, intensity, shaping) contribute most to positive treatment outcomes is still needed.

An additional area that warrants further investigation is optimal treatment duration. Studies of CIMT have not found any substantial improvements by increasing duration of daily therapy beyond three hours; however, there is no research to suggest whether similar treatment effects could be demonstrated in less time. This is an important implication given the expense of therapy, particularly during the chronic stage of aphasia. Additionally, Maher et al. (2006) reported loss of potential participants who cited the therapy schedule as a reason for deferring involvement, suggesting that the current level of treatment duration and intensity may not accommodate many individuals.

Finally, more information is needed to determine which individuals benefit most from intensive treatment schedules (Meinzer, Rodriguez, & Rothi, 2012). Meinzer and colleagues (2007) found that participants with severe aphasia benefited most from CI training, particularly for expressive language (as cited in Meinzer, Rodriguez, & Rothi, 2012). These findings suggest that individuals who are more withdrawn from communication may receive greatest benefit from intensive language stimulation (Meinzer, Rodriguez, & Rothi, 2012).

Chapter 6: Evaluation of CI Therapy in Acute Aphasia

There is a critical need to determine at which stage in aphasia rehabilitation CI-based treatment is most effective. Although there is a substantial amount of research investigating the efficacy of CI therapy with individuals with chronic stroke, research exploring the use of CI therapy with individuals in early aphasia rehabilitation is sparse. To date, only one study has been conducted with individuals in the acute stage of aphasia (1-2 months post-stroke). Kirmess and Maher (2010) carried out a case series with three individuals (HP, GA, and FOT) with aphasia resulting from left CVA. Modifications to the original treatment protocol, such as bedside administration of intervention and dividing treatment blocks into shorter sessions, were required to accommodate for medical and rehabilitation needs in the acute hospital setting. Therapy dosage ranged from 1.15 to 3 hours per day, with total therapy hours of 20 (HP), 24.5 (GA) and 30 (FOT). Therapy activities, modeled after Pulvermüller et al. (2001) and Maher et al. (2006), were delivered in group and individual settings. No constraint was employed outside of training.

Assessments were conducted at baseline and following treatment using the Norwegian Basic Aphasia Assessment (NGA) (Reinvang 1985), the Test for Reception of Grammar (TROG-2)(Bishop, 2009), subtest 7 (sentence construction) of the Verb and Sentence Test (VAST) (Bastiaanse, Edwards, Moen, & Rispins, 2002), the experimental version of subtest 54 (naming frequency) from the Psycholinguistic Assessments of Language Processing in Aphasia (PALPA) (Kay, Lesser, & Coltheart, 1999), and the Cookie Theft (CT) picture description (Goodglass

& Kaplan, 1972). Additionally, a questionnaire, consisting of a 5-point scale and open-ended questions and comments, was utilized to evaluate the participants' experience with CILT. Follow-up testing was completed at three months (HP) and six months (FOT) after intervention. High inter-rater reliability (average 92.9%) was demonstrated on all measures.

Participants demonstrated improved performance on the five language tests and six speech production subtests following treatment. Individual improvements ranged from 5.1% (GA) to 18.7% (HP) to 23.3% (FOT). Improvements on reading comprehension and written output were less substantial (range= -0.6% to 4.4%). Individual effect sizes could not be reported due to lack of normative data from the Norwegian test versions. Increase in words per minute was noted for the NGA conversational interview (HP=28%, FOT=48%, GA=6%) suggesting improvements in functional communication at the conversational level. Responses from the self-report questionnaire indicated positive experiences with the approach for all participants. Follow-up testing revealed an even greater increase in gains; however, participants continued with additional traditional therapy during the time leading up to the follow-up assessment. The role of spontaneous recovery in the acute stage of aphasia also plays a factor that could not be controlled for in this stage of rehabilitation. Increased improvement on expressive language compared to written expression, suggests that training contributed to a treatment-specific response to therapy as spoken, rather than written language, was targeted. While results were generally positive and no explicitly harmful effects were found at this early stage in rehabilitation, lack of control group limited generalization of findings.

Chapter 7: Adaptations of CI Therapy to Target Specific Language Functions

Recent studies (Szaflarski et al., 2008; Goral & Kempler, 2009; Faroqi-Shah & Virion, 2009) have utilized adaptations of CI-based therapy to target specific areas of language impairment. However, modified protocols have only been employed with a small number of participants, limiting applicability of findings.

Szaflarski and colleagues (2008) used a modified CI-based protocol containing an additional language hierarchy based on individual skill levels of three participants with moderate to severe chronic aphasia. Two of the participants presented with nonfluent aphasia. The remaining participant presented with jargon speech and moderate comprehension deficits. Language hierarchies were developed from each participant's linguistic strengths, as determined from pre-treatment testing. Individual goals targeted semantic, syntactic and phonological language production. The Boston Diagnostic Aphasia Exam-3 (BDAE-3; Goodglass, Kaplan & Barresi, 2001) was utilized to assess auditory comprehension and verbal expression pre- and post-testing. The investigators developed a mini-Communicative Activity log (mini-CAL) containing 16 questions to evaluate changes in functional communication. A linguistic analysis of the BDAE-3 fable story retell (Goodglass, Kaplan & Barresi, 2001) was conducted using the Systematic Analysis of Language Transcripts (SALT Version 8) program. Therapy sessions lasting approximately 3-4 hours a day were delivered over a span of five days. Barriers were not utilized in the therapy activities to increase naturalness of the treatment environment. Following therapy, two participants demonstrated improvements on auditory comprehension components of the BDAE-3. The investigators speculated that improvements on auditory comprehension measures may be related to intensive practice of listening during therapy activities, rather than the constraint-based approach itself. While no improvements on the expressive components of the BDAE-3 were demonstrated, linguistic analysis revealed significant increases in total number of words (31% and 95%) and number of utterances during the story retell task (57% and 75%) for two participants. Failure for the third participant to make significant gains may be attributed to higher pre-treatment severity score, suggesting that more severe impairment may contribute to poorer prognosis following therapy, particularly when comprehension deficits are present. Improvements in communication skills were not indicated by any patients on the mini-CAL questionnaire. However, lack of comprehension of questions may have limited the validity of responses.

Goral and Kempler (2009) utilized a modified CI-based treatment to train verb production in communicative contexts with an individual with chronic nonfluent aphasia (12 years post-stroke). The participant's speech consisted of mostly one-word utterances containing predominantly nouns. The goal of the study was to train verb production in the context of information exchanges, resembling conversation. A time-blocked A-B-A-B (treatment block 1 - no treatment – treatment block 2 - no treatment block) design was employed. Pre-and post-treatment assessments were conducted after each treatment block and at a 10-week follow-up assessment using the BDAE-3 (Goodglass, Kaplan & Barresi, 2001) and Cognitive Linguistic Quick Test (CLQT; Helm-Estabrooks, 2001). Measures of functional communication skills included narrative constructions regarding three personally relevant topics (i.e. career, family, favorite vacation), and naïve listener ratings completed using a 10-item Conversation Perception Questionnaire developed by the investigators. Twenty naïve listeners blinded to the experiment and unfamiliar to the participant completed the questionnaire. Therapy blocks, consisting of total 20 therapy hours, were delivered over a span of four weeks (5 hours/week over 4 weeks). Therapy tasks included a structure "go fish" task, targeting production of 57 behaviorally relevant verbs. Additional activities included a story-generation task, which did not target training of specific verbs. Task difficulty was gradually increased as the participant's skill level improved. Following treatment, significant improvements were not demonstrated on the CLQT or BDAE-3, except for the auditory comprehension subtest (increase of 17%). Post-treatment narratives revealed an increase in percentage of verbs from 3.6% at pretreatment, to 4.5% following the first treatment block and 8.6% following the second treatment block. At follow-up verb production decreased slightly to 5.5%, but remained significantly higher than pre-treatment verb production. An increased production of verb inflections and auxillary verbs was noted following therapy, as well as an increase in variety of verbs produced (13 at pretreatment; 26 at follow-up). Increase in variety of verbs produced that were not specifically trained in therapy suggests some generalization of effects. No significant changes were noted in noun production and total number of words produced. Additionally, mean ratings for the 20 naïve listeners increased from 4.4 (SD=.73) to 4.7 (SD=.67), $t(19)=-3.36$, $p=.003$. suggesting an improvement in social communication. However, given the relatively modest improvement on the questionnaire, results should be interpreted cautiously and additional research with this assessment measure is needed. Additionally, the participant attended a weekly, one-hour conversational group during the course of therapy, which may have contributed to changes in performance, as well.

Faroqi-Shah and Virion (2009) investigated the effects of using additional morphosyntactic constraints to treat individuals with agrammatic aphasia. Four participants with chronic agrammatic aphasia completed the study. Participants demonstrated relatively intact conversational comprehension and content word retrieval, but severely impaired morphosyntactic production. Two participants received conventional CILT, while the other two participants received additional constraints regarding production and judgments of tense morphology. A total of 24 therapy hours were delivered over the span of 10 days. Assessments were completed pre- and post-treatment and at a three-month follow-up. Outcome measures assessing changes in aphasia severity included the Aphasia Quotient (AQ) on the WAB-R (Kertesz, 2007), the BNT (Kaplan, Goodglass, & Weintraub, 2000), and the verb naming portion on the Object and Action Naming Battery (OANB; Druks & Masterson, 2000, Form 2, List A). Changes in morphosyntactic production were measure using the Verb Inflection Test (Faroqi-Shah, unpublished), the Cinderella narrative story, and an informal conversational sample. The modified protocol required participants to use appropriate adverbs and verb tense in their responses during the card game, and to additionally make judgments about the correctness of other players' morphosyntax. Following treatment, although improvements in overall aphasia severity were made, changes did not reach level of significance, which may be attributed to the small sample size. However, improvement on at least one standardized test was noted for all participants. Significant changes on the Verb Inflection Test were noted by the two participants who received additional morphosyntactic constraints ($p<.05$) and not by the participants who received conventional CILT. The structure of the test closely resembled the morphosyntactic constraints incorporated in their therapy, which gave participants increased advantage compared to the participants who received traditional CILT. Narrative measures did not yield consistent results across participants, with no distinct advantage noted for the participants with additional constraints, suggesting a lack of generalization to discourse. Results from the study suggest that morphosyntactic deficits may be more resistant to changes induced by CI based therapy. Additional investigation regarding which participant factors predict more positive prognosis following CI-based therapy approaches is warranted.

Chapter 8: Alternative Methods of Treatment Delivery

There is a need to increase treatment intensity for treating individuals with chronic aphasia (Kelly, Brady, & Enderby, 2010). Given the financial limitations of treating individuals in the chronic stages of aphasia, increasing availability of treatment to individuals through alternate methods of delivery (e.g. computer programs, layperson training) is critical. While computerized treatment has been used effectively with individuals with chronic aphasia (Wallesch & Johannsen-Horbach, 2004; Wertz & Katz, 2004**)**, many programs are unable to adapt and modify tasks to fit individual needs and continue to require presence of a therapist (Meinzer, Rodriguez, & Rothi, 2012). Alternatively, laypersons may be trained to provide therapy as an adjunct to professional intervention to increase treatment intensity and reduce treatment cost.

The effectiveness of training laypersons to deliver CIAT was explored in a controlled trial conducted by Meinzer, Streiftau, and Rockstroh (2007). Twenty participants with chronic aphasia were randomly assigned to receive CI-based therapy delivered by either experienced therapists or trained laypersons. Participants were identified as having moderate to severe fluent and nonfluent aphasia. For practical purposes, participant relatives were selected as laypersons to be trained to deliver therapy. For the first two days of therapy, the laypersons received supervision from experienced therapists while delivering therapy. Therapy was led independently by the laypersons for the remaining eight days of therapy. Daily meetings between the laypersons and therapists were arranged to discuss and troubleshoot any problems encountered (as cited in Meinzer, Rodriguez, & Rothi, 2012).

Both groups demonstrated significant improvements on the AAT, with no significant between-group differences found on any subtests. Functional communication was not assessed, nor was layperson performance evaluated. Small sample size was an additional limitation. Preliminary findings from this study suggest that layperson training is a viable means of delivering CIAT to individuals with chronic stroke.

Chapter 9: Pharmacotherapy in Conjunction with CI Therapy

Drugs have been used to modulate neurotransmitter systems to directly and indirectly influence language functioning by increasing arousal, attention and working memory (Meinzer, Rodriguez, & Rothi, 2012). Particularly, drugs affecting gutaminergic, monoaminergic, and cholingergic transmitters have been shown to improve cognitive and language abilities in individuals with strokes (Meinzer, Rodriguez, & Rothi, 2012).

Berthier and colleagues (2009) suggested an additional benefit of utilizing pharmacotherapy in combination with CIAT to treat individuals with chronic aphasia (time post stroke> 1 year). An N-methyl-D-aspartate receptor antagonist (memantine) was selected for investigation, which previously was shown to lead to improved treatment outcomes with individuals with mild-to-moderate vascular dementia (Berthier et al., 2009). Twenty-eight individuals with chronic aphasia participated in a randomized, double-blinded, placebo-controlled, parallel-group study. Participants were randomly assigned to either a mematine (n=14) or a placebo (n=14) treatment group. The CAL (Pulvermüller et al., 2001) and Western Aphasia Battery-Aphasia Quotient (Kertesz, 2007) were used to evaluate language functioning and overall aphasia severity at baseline and at intervals 16, 18, 20, 24, and 48 weeks of treatment. Drugs were delivered over a period of 20 weeks, followed by a washout period during weeks 20 to 24. CI-based therapy was delivered during weeks 16 through 18 in conjunction with pharmacologic treatment. An open-label phase, in which all participants received memantine, was offered at the end of 24 weeks. Significant improvements on the Western Aphasia

Battery-Aphasia Quotient and CAL were found for both groups following CIAT, with more pronounced improvements demonstrated by the memantine group compared to the placebo group. Improvements were maintained at the washout assessment and in long-term follow-up assessment at 48 weeks. No adverse drug effects were reported. The investigators speculated that memantine may increase use-dependent neuroplasticity stimulated by CIAT. However, additional replications using larger participant samples are needed for more conclusive information on the benefits of pharmacologic treatment in conjunction with intensive language therapy, such as CIAT.

Chapter 10: Findings from Functional Imaging

Magnetic source imaging studies conducted with both humans and animals have suggested that cortical reorganization may be associated with use-dependent therapy approaches. Following an influential study by Merzenich et al. (1984) demonstrating use-dependent cortical reorganization in monkeys using intracortical microstimulation (ICMS), Elbert and colleagues (1995) conducted a human imaging study involving musicians. Imaging revealed that the cortical somatosensory representation of the fingers of the left hand was larger in string players compared to nonmusician controls. Similar findings of increased cortical representation were noted for blind Braille readers, who utilize three fingers on both hands to read, compared to controls (Sterr et al., 1998). Concurrent results from both animal and human imaging studies suggest that the size and nature of cortical representation of a given body part is directly influenced by the use of that body part (Taub, Crago, & Uswatte, 1998). These studies suggest that an increase in use of an affected limb may result in use-dependent increase in amount of cortical representation of that extremity, which in turn serves as a neurological basis for increased functioning of that extremity (Taub, Crago, & Uswatte, 1998).

There is limited research investigating whether positive treatment effects for intervention are also associated with changes in neural organization for individuals with chronic aphasia (Meinzer, Rodriguez, & Rothi, 2012). CI-based therapy has recently been employed in functional imaging studies to explore the effects of treatment-induced neural reorganization for individuals beyond the period of spontaneous recovery (i.e. >1 yr post-stroke) (Meinzer, Rodriguez, & Rothi, 2012).

Single- and multiple-case studies (Meinzer, Obleser, Flaisch, Eulitz, & Rockstroh, 2007; Breier, Maher, Novak, & Papanicolaou, 2006; Breier, Maher, Schmadeke, Hasan, & Papanicolaou, 2007) involving individuals with chronic aphasia have provided evidence of neural reorganization following CI-based therapy. However, conclusions regarding the nature and pattern of neural changes cannot be drawn from such small-scale samples (Meinzer, Rodriguez, & Rothi, 2012).

Several group studies have been conducted to establish generalizable conclusions about treatment-induced neural reorganization following CI-based therapy. Meinzer and colleagues (2004) conducted the first group study exploring the functional effects of intensive therapy in individuals with chronic aphasia. Twenty-eight participants with mild-to-moderate nonfluent aphasia were treated using CI-based therapy (n=18) or MOAT (n=12). To minimize the effects of spontaneous recovery as a confounding variable, all participants selected were in the chronic stage of aphasia (>12 months post-stroke). Average test performance on the AAT (Huber, Poeck, Weniger, Willmes, 1983) increased for the participant groups following the two-week treatment period. Functional activity was assessed using a magnetoencephalography (MEG) scan at baseline and following treatment to examine patterns of slow wave activity. Increased slow wave activity (delta frequency range 1-4 Hz) is typically found in areas surrounding structural damage in the brain and is often a marker for dysfunctional neural networks. Twenty-six of the 28 participants demonstrated significant (r=.60) changes in slow wave activity in the vicinity of the lesion site following treatment. Magnitude of change in activity in perilesional activities was more prominent in participants who demonstrated significant compared to minor improvements on one or more subtests of the AAT. Results suggest that CI-based approaches can contribute to reorganization of neural networks responsible for language functioning for individuals with chronic aphasia.

A follow-up study was conducted by Meinzer and colleagues (2008) to gain further information regarding the significance of functional changes in brain activity following treatment. MEG scans from 11 participants with chronic aphasia (>6 months post-stroke) were collected prior to treatment to determine individual regions-of-interest (ROIs) where slow wave brain activity was high. Typically, ROIs are clustered in the areas surrounding the infarct in the left hemisphere. Participants' brain activity during an overt naming task was evaluated at baseline and directly following CIAT using functional magnetic resonance imaging (fMRI). Language functioning was additionally assessed using the profile score on the AAT (Huber, Poeck, Weniger, Willmes, 1983) to evaluate aphasia severity. Significant decreases in aphasia severity, as measured by the profile score and subtests of the AAT, were found following treatment. Functional imaging revealed improvements on the overt picture-naming task were correlated with increased activity in ROIs and in the lesion homologue in the right hemisphere. Notably, lower pre-training performance on naming tasks was associated with more significant improvements following training ($r=.73$, $p=.02$). Moreover, lower functioning individuals demonstrated more prominent increases in activity in ROIs ($r=.57$, $p=.10$), suggesting that individuals with more severe deficits may benefit more substantially from intensive treatment. Although pre-treatment naming performance directly influenced language outcomes, aphasia duration did not restrict functional changes, suggesting that neural reorganization can occur beyond the acute stage of stroke. However, as follow-up data was not collected, long-term effects of reorganization remain unknown. Additional limitations include small sample size and lack of control group to explore the effects task repetition on activation patterns.

There is a lack of conclusive information regarding the role of brain activity in each hemisphere in supporting recovery for individuals with chronic stroke. Richter, Miltner and Straube (2008) conducted the largest fMRI study investigating patterns of activation in right-hemispheric areas and left perilesional areas before and after CIAT. Sixteen participants with chronic nonfluent aphasia and eight healthy controls were assessed using functional imaging during a word-reading (REA) and word-stem completion (COM) tasks. At baseline assessment, both control and aphasic participants exhibited right hemisphere activation during tasks. However, stronger activations in the right inferior frontal gyrus/insula (IFG/IC) activity during REA and precentral gyrus during COM was observed in participants with aphasia compared to control subjects. Significant changes in activation patterns were not observed following CIAT. However, improvement on behavioral measures of language functioning was positively correlated with a relative decrease in activation in right hemispheric areas. Moreover, greater initial activation in right hemispheric areas was associated with more favorable treatment outcomes. Lack of treatment effects for left perilesional areas may be attributed to decreased reliability analyzing left hemispheric ROIs due to variation in lesions across participants. In addition to variations in lesions, some participants with aphasia also presented with speech comprehension deficits, which may have additionally influenced treatment outcomes.

Pulvermüller, Haul, Zohsel, Neininger, and Mohn (2005) explored changes in bilateral brain activity by assessing strength of event-related potentials (ERPs) in nine participants with chronic aphasia before and after CIAT. Event-related potentials were measured using electroencephalography during a lexical decision task, which evaluated latency time following visual presentations of words and nonsense pseudowords. Following therapy, early word evoked potentials (latency 250-300 ms) increased significantly in strength, while no change was observed in potentials evoked by pseudowords. Bilateral cortical activation in areas of language functioning, including the left posterior temporal and right frontal corticies, was observed and significantly correlated with improvement on behavioral measures of language functioning (e.g. Token Test; Huber, Poeck, Weniger, Willmes, 1983). Results suggest that cortical reorganization in both hemispheres is associated with improved language functioning following CIAT.

Finally, a recent study investigated the relationship between behavioral measures of language improvement and neurophysiologic responses to CILT, as measured using MEG (Breier et al., 2009). Twenty-three participants with chronic aphasia were evaluated prior to and immediately following therapy, and at a three-month follow-up assessment. At each assessment period, participants' language was evaluated in terms of percentage of correct information units (CIUs). MEG scanning sessions were conducted during a word recognition memory task for spoken words to evaluate number of late dipoles normalized to total activation.

Following treatment, participants were distributed into three groups based on behavioral measures of performance: 1) those who demonstrated significant improvement of >24% CIUs or more from pre-CILT testing that was maintained at follow-up 2) participants that improved significantly but did not maintain performance at follow-up and 3) those who did not demonstrate significant improvements over pre-CILT performance following therapy or at follow-up. Participants who failed to maintain treatment gains at follow-up demonstrated increased right hemisphere activation compared to other participants at all MEG scanning sessions. Participants who maintained gains at follow-up demonstrated increased left temporal activation following CILT, while participants who failed to make significant gains on behavioral measures following therapy exhibited comparably greater left parietal activation. Results suggest that right hemisphere activation may play a role in improved language recovery temporarily, but does not provide stability over time. Participation of left perilesional areas in neural reorganization may be critical for long-term stability. Greater lesion size in participants who failed to make gains was noted as a potential confounding variable in the study. Additionally, given that CILT is primarily focused on speech production rather than comprehension, the study is limited in that neurophysiologic responses were collected during a convert, rather than overt task.

In conclusion, studies suggest that CI-based approaches can contribute to changes in neural organization for individuals with chronic stroke. However, lack of standardization across studies, including differences in therapy tasks (e.g. covert vs. overt) and treatment measures, limits the clarity of findings regarding patterns of brain activation associated with successful treatment outcomes. In addition, differences across participant samples, including aphasia type (e.g. nonfluent vs. fluent), comorbid deficits (e.g. impaired language comprehension), and lesion size and location were not controlled across studies, limiting applicability of results. In general, findings from these studies suggest that increased right-hemisphere activation during language production tasks is associated with less favorable treatment outcomes (Meinzer, Rodriguez, & Rothi, 2012). Additionally, increased activity in perilesional areas in the left hemisphere and down-regulation of activity in the right hemispheric areas appears to be associated with more positive treatment outcomes (Meinzer, Rodriguez, & Rothi, 2012). Further research is warranted in this domain to increase understanding of the underlying mechanisms of recovery for individuals with chronic aphasia to better predict prognosis (Meinzer, Rodriguez, & Rothi, 2012).

Chapter 10: Conclusion

While the principles of learned nonuse established in animal studies were applied fairly directly to human motor rehabilitation, the application of CI-based therapy for aphasia is less straightforward. There is modest evidence to suggest that constraint-based therapy is effective in treating language deficits in individuals with acute (Kirmess and Maher, 2010) and chronic aphasia (Pulvermüller et al., 2001; Meinzer et al., 2005; Maher et al., 2006). Modest gains have been demonstrated on standardized language tests and/or measures of functional communication aphasia (Pulvermüller et al., 2001; Maher et al., 2006); however, consistent results have not been demonstrated across studies. Follow-up data also is lacking across studies, providing only limited evidence (Meinzer et al., 2005; Maher et al., 2006) to suggest long-term benefits of CI-based therapy. Optimal treatment intensity and timing in the rehabilitation process remain ambiguous. Additionally, inconsistencies in participant samples across studies reduce clarity regarding which individual characteristics (e.g. aphasia severity/type) predict positive outcomes following therapy.

CI-based therapy has been compared to other high-intensity approaches, yielding similar results in terms of improvement, particularly when an additional family training component was included (Meinzer et al., 2005). However, the high treatment intensity may not accommodate many individual's schedules (Maher et al., 2006). Financial implications of high-intensity therapy in the chronic stages of therapy also may limit application of the approach to clinical settings.

Modifications to the protocol have been utilized to address individual areas of language impairment. Inconsistent gains were found across participants, with limited gains observed on measures of functional communication (Szaflarski et al., 2008) or measure of connected speech (Faroqi-Shah & Virion, 2009). Replication of studies on a larger scale are needed to determine effectiveness of modified protocols.

Studies involving functional imaging (Pulvermüller et al., 2005; Breier et al., 2009; Richter, Miltner and Straube 2008) suggest that CI-based therapy can contribute to treatment-dependent neural reorganization, however, the nature and pattern of changes remain unclear. Inconsistencies across studies, including variations in treatment tasks during neuroimaging, treatment measures, and patient characteristics (e.g. lesion size and location) limits generalization of findings. In conclusion, evidence of the effectiveness of CI-based therapy for aphasia remains preliminary, but promising. Future research should incorporate large-scale randomized controlled studies with well-defined participant samples to increase understanding of optimal treatment timing and participant characteristics that predict positive prognosis.

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